

IN THE UNITED STATES DISTRICT COURT
FOR THE SOUTHERN DISTRICT OF TEXAS
HOUSTON DIVISION

BEN N. BROWN, SR.

Plaintiff,

V.

SHELL OIL COMPANY, SHELL
CHEMICAL, L.P., RADIATOR
SPECIALTY COMPANY, AND JOHN
DOES 1 THROUGH 250, INCLUSIVE,

Defendants.

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C.A. NO. 4:08-CV-00413

**SHELL DEFENDANTS’ BRIEF IN SUPPORT OF THEIR
MOTION TO EXCLUDE PLAINTIFF’S CAUSATION EXPERTS**

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TABLE OF CONTENTS

	<u>Page</u>
TABLE OF AUTHORITIES	v
TABLE OF EXHIBITS	vi
I. SUMMARY OF THE ARGUMENT	1
II. NATURE AND STAGE OF THE PROCEEDING	2
III. STATEMENT OF MATERIAL FACTS	3
IV. STATEMENT OF THE ISSUES	5
V. STANDARD OF REVIEW	5
VI. ARGUMENTS	7
A. Background Principles	7
1. General Causation Is Premised Upon Applicable Epidemiology	7
2. Relevant Epidemiology Must Address Plaintiff’s Specific Disease	7
B. Plaintiff’s Experts’ General Causation Opinions Are Unreliable and Should Be Excluded	8
1. There Is No Evidence of General Causation Between Exposure to Crude Oil, Natural Gas Condensate, Solvents, or Paints and Multiple Myeloma	8
2. Plaintiff’s Experts’ General Causation Opinions of A Causal Link Between Exposure to Benzene and Multiple Myeloma Are Not Generally Accepted	9
a. Authoritative Scientific Bodies Do Not Establish A Causal Link Between Benzene and Multiple Myeloma	9
b. The Health Watch Cohort Study Found No Causal Association	12
c. Multiple Other Studies Show No General Causation	13
d. Scientific Reviews of the Literature Show No General Causation	13
e. The Epidemiology Is Supported By Clinical Evidence	14
3. Specific Opinions of Plaintiff’s Experts	15
a. Dr. Infante’s Opinions	15

b. Dr. Harrison's Opinions.....	18
c. Dr. Butler's Opinions	18
VII. CONCLUSION	19
CERTIFICATE OF SERVICE	21

TABLE OF AUTHORITIES

FEDERAL CASES

<i>Allen v. Pennsylvania Engineering Corp.</i> , 102 F.3d 194 (5th Cir. 1996)	passim
<i>Daubert v. Merrell Dow Pharmaceuticals</i> , 509 U.S. 579 (1993).....	passim
<i>General Electric Company v. Joiner</i> , 522 U.S. 136 (1997).....	6, 7
<i>Knight v. Kirby Inland Marine Inc.</i> , 482 F3d 347, 351 (5th Cir. 2007)	passim
<i>Leija v. Penn. Mar.</i> , Civ. Action No. 06-10489, 2009 U.S. Dist. LEXIS 8539, *6 (E.D. La. Jan. 23, 2009)	7
<i>Moore v. Ashland Chem. Inc.</i> , 151 F.3d 269, 276 (5th Cir. 1998)	5, 6
<i>Wright v. Williamette</i> , 91 F.3d 1105, 1106 (8th Cir. 1996)	7

STATE CASES

<i>Henricksen v. Conoco Phillips Company</i> , No. CV-07-224-JLQ, at *15	8, 14
<i>Hutchinson v. Shah</i> , 648 So.2d 1108, 1112 (La. App. 5th Cir. 1998)	2, 5
<i>Merrell Dow Pharm., Inc. v. Havner</i> , 953 S.W.2d 706, 716 (Tex. 1997).....	7, 17

FEDERAL RULES

FED. R. EVID. 702.....	6
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TABLE OF EXHIBITS

Exhibit	Description
A	Excerpts of Plaintiff's Deposition from January 7, 2009
B	Report of Kenneth Mundt, Ph.D.
C	Report of Ethan Natelson, M.D.
D	Report of Sheila Butler, M.D.
E	Report of Robert Harrison, M.D., M.P.H.
F	Report of Peter Infante, D.D.S., Dr. Ph.H.
G	Reference Manuel
H	Selected Articles
I	Statements of Authoritative Scientific Bodies
J	Report of David Pyatt, Ph.D
K	Plaintiff's Response to Interrogatory No. 13
L	State and Unpublished Cases

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[illegible]

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**SHELL DEFENDANTS' BRIEF IN SUPPORT OF THEIR
MOTION TO EXCLUDE PLAINTIFF'S CAUSATION EXPERTS**

Shell Defendants file this Brief in Support of their Motion to Exclude Plaintiff's Causation Experts.

I. SUMMARY OF THE ARGUMENT

Plaintiff Ben N. Brown Sr.'s medical causation theory is premised on the assumption that his work with crude oil, natural gas condensate, solvents, and paints exposed him to benzene and caused his multiple myeloma. Three of the Plaintiff's retained experts—Peter Infante, PhD, Robert Harrison, MD, and Sheila Butler, MD—each opine that benzene causes multiple myeloma, in essence conflating Plaintiff's limited exposure to products that may contain small amounts of benzene with exposure to pure benzene products. An assumption of significant benzene exposure of any kind in this case is improper. Moreover, as an upstream offshore oil production worker, the outdoor environment in which Plaintiff worked would have drastically reduced the potential for exposure to even the small amounts of benzene that might have been present. Nevertheless, despite Plaintiff's experts' inaccurate characterization of Plaintiff's

exposure, the vast majority of the epidemiology studies establish no association between benzene exposure of any kind or quantity and multiple myeloma. The lack of epidemiology linking crude oil and other hydrocarbons to multiple myeloma is particularly telling.

In any toxic tort case relevant and reliable evidence of general causation is required. *Knight v. Kirby Inland Marine Inc.*, 482 F3d 347, 351 (5th Cir. 2007). “General causation is whether a substance is capable of causing a particular injury or condition in the general population, while specific causation is whether a substance caused a particular individual’s injury.” *Knight*, 482 F3d at 351. Evidence concerning specific causation is admissible only as a follow up to admissible general causation evidence. *Knight*, 482 F3d at 351. Plaintiff is required to prove general and specific causation through scientifically and medically reliable evidence. *Knight*, 482 F3d at 351; *Hutchinson v. Shah*, 648 So.2d 451, 452 (La. App. 1st Cir. 1994) (attached as Exhibit L).

Defendants Shell Oil Company and Shell Chemical, L.P. (collectively “Shell Defendants”) challenge the scientific reliability of Drs. Butler, Harrison, and Infante’s (Plaintiff’s Experts) general causation opinions pursuant to Federal Rule of Evidence 702, offered on behalf of Plaintiff Ben N. Brown, Sr. These expert opinions are neither relevant nor reliable under *Daubert v. Merrell Dow Pharmaceuticals*, 509 U.S. 579 (1993), *Allen v. Pennsylvania Engineering Corp.*, 102 F.3d 194 (5th Cir. 1996) and *Knight v. Kirby Inland Marine, Inc.*, 482 F.3d 347 (5th Cir. 2007).

II. NATURE AND STAGE OF THE PROCEEDING

In his First Amended Complaint, Plaintiff alleges that Shell Defendants manufactured sold, or distributed harmful products which caused his multiple myeloma. *See* R. Doc. 5. Specifically, Plaintiff alleges that he was exposed to “Crude Oil, Crude Oil and natural gas

associated produced water, liquid condensate, waxes, tars, sands, scale, solvents, reformat, raffinates, Liquid Wrench, Naptha, Ed-40, N.O.R.M. (Naturally Occurring Radioactive Materials), radiation from examination of steel tubular goods and pipes, structures, etc., paints asphalt paints and mastics, adhesives, glues and anti-corrosion materials” which caused his multiple myeloma. *See* Exhibit K, Response to Interrogatory 13. Plaintiff’s tort claims are negligence and product liability under Louisiana law, and strict product liability under the Restatement (Second) of Torts. *See* R. Doc. 5, paragraph 11.

To prove medical causation, Plaintiff has retained five experts. *See* R. Doc. 51. Only three of the experts’ reports—the reports of Drs. Butler, Harrison and Infante—address general causation.

On January 23, 2009, Plaintiff filed an opposed Motion for Leave to Amend his complaint to add new parties and to plead a fundamentally different case with new claims. Shell Defendants filed a Response to Plaintiff’s Motion for Leave to Amend on February 10, 2009. This Court has not ruled on Plaintiff’s opposed Motion for Leave to Amend.

III. STATEMENT OF MATERIAL FACTS

Plaintiff is a 66 year old man who was diagnosed with multiple myeloma. *See* R. Doc. 5, paragraph introduction; Exhibit A, Jan. 7, 2009 10:13-17, exhibit 1 to depo. (Plaintiff’s date of birth redacted). Plaintiff alleges his multiple myeloma was caused while he worked as a maintenance worker and lease operator at Shell Oil Company and Shell Offshore Inc. *See* R. Doc. 56, paragraph 4; R. Doc. 56 attachment 1, paragraph 8. Between 1968 and 1992, for approximately 24.5 years, Plaintiff worked for Shell Oil and Shell Offshore in the Outer Continental Shelf, in Louisiana waters. *See* R. Doc. 56, paragraph 4; R. Doc. 56 attachment 1, paragraph 8. During those 24.5 years, Plaintiff worked as follows:

- from 1968 to 1969 (one year) as a laborer in the oil fields also referred to as “maintenance man A”
- from 1969 to 1974 (5 years) for three years as a “maintenance man B” on a spud barge and for two years as a paraffin cutter on a jack up barge
- from 1974 to 1990 (16 years) he worked as a lease operator in charge of fixed platforms
- from 1990-1992 (one year) as an office assistant.

See R. Doc. 56, paragraph 4; R. Doc. 56 attachment 1, paragraph 8; Exhibit A, Jan. 7, 2009, 50:9-14, exhibit 1 to deposition. During that time, Plaintiff worked outdoors. *See* Exhibit A, Plaintiff’s Feb. 11, 2009 Depo. 40:4-20.

Plaintiff alleges that he was exposed to crude oil, natural gas condensate, solvents, and paints that caused his multiple myeloma. *See* Exhibit K. He does not allege that he was exposed to pure benzene.

In support of their Brief, Shell Defendants attached and incorporate the following exhibits:

- Exhibit A: Excerpts of Plaintiff’s Deposition
from January 7, 2009 and February 11, 2009
- Exhibit B: Report of Kenneth Mundt, Ph.D.
- Exhibit C: Report of Ethan Natelson, M.D.
- Exhibit D: Report of Sheila Butler, M.D.
- Exhibit E: Report of Robert Harrison, M.D., M.P.H.
- Exhibit F: Report of Peter Infante, D.D.S., Dr. P.H.
- Exhibit G: Reference Manual
- Exhibit H: Selected Articles
- Exhibit I: Statements of Authoritative Scientific Bodies
- Exhibit J: Report of David Pyatt, Ph.D

Exhibit K: Plaintiff's Response to Interrogatory No. 13

IV. STATEMENT OF THE ISSUES

The issue is whether this Court should grant Shell Defendants' Motion to Exclude The testimony of Plaintiff's Experts when

- Plaintiff's Experts' general causation opinions are not generally accepted and contrary to the vast weight of scientific evidence;
- there is no evidence of general causation between exposure to crude oil, natural gas condensate, solvents, or paints and multiple myeloma; and
- the underlying data and studies on which Plaintiff's Experts rely are inapplicable to the facts of this case.

V. STANDARD OF REVIEW

A plaintiff in a toxic tort case must, under Louisiana law, establish medical causation through expert testimony. *Hutchinson*, 648 So.2 at 452. For expert testimony to be admissible in federal trials, however, it must meet the scientific relevance and reliability tests set forth in *Daubert* and *Knight*. See *Daubert*, 509 U.S. at 589; *Knight*, 482 F3d 347 at 351.

In *Daubert*, the Supreme Court recognized that Rule 702 displaced the *Frye* evidentiary test of general acceptance. Instead, scientific evidence would be admissible if it would "assist the trier of fact to understand the evidence or to determine a fact in issue." FED. R. EVID. 702. However, in order to qualify as scientific knowledge, an inference or assertion must be supported by the scientific method. Evidentiary reliability, therefore, is based upon scientific validity. *Moore v. Ashland Chem. Inc.*, 151 F.3d 269, 276 (5th Cir. 1998). Moreover, the expert's methodology must be scientifically valid. See *Knight*, 482 F3d at 351. The Supreme Court has provided a non-exhaustive list of factors, such as testability, peer review, potential error rate, and general acceptance to guide courts in the reliability analysis. *Daubert*, 509 U.S. at 592-595.

Rule 702's "helpfulness" standard also requires that scientific evidence be relevant, *i.e.*, there must be an adequate "fit" between the scientific evidence and the facts in the case. *Daubert*, 509 U.S. at 592-595; *see Knight*, 482 F.3d at 355 (to be relevant the reasoning must be applied properly to the facts of the case); *see also Moore*, 151 F.3d at 276 ("[t]o support a conclusion based on such reasoning, the extrapolation or leap . . . must be reasonable and scientifically valid") (internal citations omitted).

Although a *Daubert* analysis is centered on an expert's methodology, an expert's conclusions may also be challenged. As was stated by the Supreme Court in *General Electric Company v. Joiner*:

Respondent points to *Daubert's* language that the "focus, of course, must be solely on principles and methodology, not on the conclusions that they generate. . . . " But conclusions and methodology are not entirely distinct from one another. Trained experts commonly extrapolate from existing data. But nothing in either *Daubert* or the Federal Rules of Evidence requires a district court to admit opinion evidence that is connected to existing data only by the *ipse dixit* of the expert. A court may conclude that there is simply too great an analytical gap between the data and the opinion proffered. That is what the District Court did here, and we hold that it did not abuse its discretion in so doing.

522 U.S. 136, 146 (1997) (citations omitted).

Once expert testimony is challenged, the proponent of the expert testimony bears the burden of establishing both its relevance and reliability under Rule 702. *See Moore*, 151 F.3d at 276. *Daubert* further holds that admissibility under Rule 702 is governed by Rule 104(a), which requires the judge to conduct preliminary fact-finding and assess whether "the reasoning or methodology underlying the testimony is scientifically valid and whether that reasoning or methodology properly can be applied to the facts in issue." *Daubert*, 509 U.S. at 592-595. A trial court's *Daubert* ruling is reviewed under an abuse of discretion standard. *Joiner*, 522 U.S. at 146.

VI. ARGUMENTS

A. Background Principles

1. General Causation Is Premised Upon Applicable Epidemiology

Epidemiology, the branch of medicine and public health that studies health outcomes and diseases in populations, is relied upon to establish general causation in legal cases. *See Merrell Dow Pharm., Inc. v. Havner*, 953 S.W.2d 706, 716 (Tex. 1997) (citing cases from various jurisdictions); Exhibit B, Report of Kenneth Mundt, PhD (“Mundt Report”) at 4. The general causation question in this case is whether the chemicals to which Plaintiff was exposed caused his multiple myeloma. Plaintiff’s retained experts, Drs. Harrison, Infante and Butler, each opine that Plaintiff’s occupational benzene exposure can generally cause multiple myeloma.

2. Relevant Epidemiology Must Address Plaintiff’s Specific Disease

Epidemiology that establishes that a particular chemical is capable of causing *some* disease is irrelevant under a *Daubert* analysis if that disease is not the one the Plaintiff has. *See Allen*, 102 F.3d at 196. In the case of benzene, epidemiology establishes a causal link between benzene and a particular type of leukemia, AML, but not multiple myeloma.¹

¹ A reliable general causation analysis also recognizes that even if a substance is capable of causing a particular disease, the amount of exposure must be considered. *Allen v. Penn. Eng’g Corp.*, 102 F.3d 194, 199 (5th Cir. 1996) (“[s]cientific knowledge of the harmful level of exposure to a chemical is required”); (citing to *Wright v. Williamette*, 91 F.3d 1105, 1106 (8th Cir. 1996) (“a plaintiff in a toxic tort case *must prove the levels of exposure that are hazardous to human being generally* as well as the plaintiff’s actual level of exposure to the defendant’s toxic substance before he or she may recover”) (emphasis added)); *Leija v. Penn. Mar.*, Civ. Action No. 06-10489, 2009 U.S. Dist. LEXIS 8539, *6 (E.D. La. Jan. 23, 2009) (plaintiff’s causation expert had no evidence of harmful exposure).

It necessarily follows, however, that if there is no evidence of *any* connection between a disease and a chemical, the question of how much of a chemical is required to generally cause the disease is moot. This is the case here.

3. Relevant Epidemiology Must Address The Right Product and Exposure

Epidemiology must also address the right product to be applicable in a given case. Exposures in refineries are different from exposures in outdoor work environments such as oil platforms. Exposures to benzene are different from exposures to products containing small amounts of benzene.

B. Plaintiff's Experts' General Causation Opinions Are Unreliable and Should Be Excluded

1. There Is No Evidence of General Causation Between Exposure to Crude Oil, Natural Gas Condensate, Solvents, or Paints and Multiple Myeloma

All benzene exposures are not the same. *See Henricksen, v. Conoco Phillips Company*, No. CV-07-224-JLQ, at *15 (E.D. Washington February 11, 2009) (attached as part of Exhibit L). Plaintiff's potential exposure to benzene was primarily his exposure to crude oil, as well as natural gas condensate, solvents, and paints. As Dr. Kenneth Mundt describes in his report, the epidemiology does not support a connection between these products and multiple myeloma. *See Exhibit B, Report of Kenneth Mundt PhD ("Mundt Report")* at 5-8.

For example, most studies suggest the highest associations of AML when the exposures of benzene are extremely high, *e.g.* the Pliofilm workers exposed to almost pure benzene. *See Exhibit C, Report of Ethan Natelson ("Natelson Report")* at 3. Similarly, Glass, et al., who have found that benzene at relatively lower amounts might cause AML, also conclude that health effects are more likely when the benzene is found in pure form and not in a dilute form of another product, such as gasoline. *See Exhibit H, Glass Study* at 573.

The benzene content of hydrocarbon mixtures such as crude oil and fuels is low. *See Exhibit H, Glass Study*, 569; *see also Exhibit J, Report of David Pyatt, Ph.D. ("Pyatt Report")* at 10 (diesel fuel). Dr. Mundt has determined that no epidemiology supports general causation of

multiple myeloma from crude oil. Exhibit B, Mundt Report at 5-8. Moreover, IARC has never found, for example, that crude oil is carcinogenic. *See* Exhibit F, Report of Peter Infante, PhD (“Infante Report”) at 14. As discussed in greater detail *infra*, none of the few inapplicable studies (e.g., Kirkeleit, Delzell, and Divine & Hartman) which Plaintiff’s experts cite establish a connection between exposure to crude oil, natural gas condensate, paints, or solvents and multiple myeloma. In fact, the literature does not support a connection between even pure benzene and multiple myeloma.

2. Plaintiff’s Experts’ General Causation Opinions of A Causal Link Between Exposure to Benzene and Multiple Myeloma Are Not Generally Accepted

“Peer review” and “general acceptance” are two of the suggested criteria for evaluation under a *Daubert* Rule 702 analysis. However, the “peer reviewed” literature, the conclusions of authoritative scientific bodies, scientific reviews of the available epidemiology, and the vast majority of the literature suggests that the general causation opinions of Drs. Infante, Harrison and Butler are not generally accepted within the scientific community.

a. Authoritative Scientific Bodies Do Not Establish A Causal Link Between Benzene and Multiple Myeloma

Unlike many other chemicals, benzene has been widely studied in various occupational populations. Exhibit B, Mundt Report at 5-6. Therefore, many authoritative scientific and regulatory bodies have reviewed which health effects may be linked to benzene exposure. The uniform lack of acceptance of a causal relationship between benzene and multiple myeloma by the United States Environmental Protection Agency (“EPA”), United States Department of Health and Human Services’ Agency for Toxic Substances and Disease Registry (“ATSDR”), World Health Organization (“WHO”), Institute of Medicine (“IOM”), and National Institutes of Health (“NIH”) is powerful, and, in this case, conclusive. *See Allen*, 102 F.3d at 196 (relying on

the “weight of the evidence” analysis used by organizations such as the WHO’s International Agency for Research on Cancer (“IARC”), Occupational Safety and Health Administration (“OSHA”), and the EPA to rate the carcinogenicity of various substances in humans).

i. The EPA And ATSDR Find No Link Between Benzene/Multiple Myeloma

The EPA has characterized benzene as a known human carcinogen, but only for acute myelogenous lymphoma (AML or ANLL). As the EPA states:

Benzene is a known human carcinogen based upon evidence presented in numerous occupational epidemiological studies. Significantly increased risks of leukemia, chiefly acute myelogenous leukemia (AML), have been reported in benzene-exposed workers in the chemical industry, shoemaking, and oil refineries. . . .

Exhibit I, U.S. EPA Integrated Risk Information on Benzene, available at

<http://www.epa.gov/iris/subst/0276.htm>. Furthermore, the EPA explains that the evidence for another form of leukemia, chronic lymphocytic leukemia (“CLL” or “CNLL”) is much more tenuous than the AML evidence. By contrast, multiple myeloma is not even defined as being “suggestively” linked to benzene exposure:

All of the epidemiological studies referred to above have some methodological problems, i.e., confounding exposures, lack of sufficient power, and other limitations, but the consistent excess risk of leukemia across all of these studies argues that such problems could not be entirely responsible for the elevated risks of cancer. Most of these epidemiologic and case studies have been reviewed in peer-reviewed publications (IARC, 1982; ATSDR, 1997; U.S. EPA, 1998). They provide clear evidence of a causal association between exposure to benzene and ANLL. The evidence is suggestive with respect to CNLL and CLL.

Exhibit I, U.S. EPA Integrated Risk Information on Benzene.

The ATSDR does not link benzene exposures with an increased risk of multiple myeloma. Rather, it states “[e]xposure to benzene has been associated with development of a

particular type of leukemia called acute myelogenous leukemia (AML).” Exhibit I, ATSDR Public Health Statement on Benzene, available at

<http://www.atsdr.cdc.gov/toxprofiles/phs3.html#bookmark05d>.

ii. Other Authoritative Bodies Are Consistent with the EPA and the ATSDR

The WHO has also determined that the epidemiology literature is insufficient to establish benzene as a cause of any cancer other than AML:

It is established that human exposure to commercial benzene or benzene-containing mixtures can cause damage to the haematopoietic system, including pancytopenia. The relationship between benzene exposure and the development of acute myelogenous leukemia has been established in epidemiological studies. Reports linking exposure to benzene with other malignancies were considered to be inadequate.

Exhibit I, World Health Organization, IARC Monograph on Benzene, available at <http://monographs.iarc.fr/ENG/Monographs/vol29/volume29.pdf>. The American Cancer Society echoes the conclusions of the EPA and IARC and the WHO, stating that “the evidence linking benzene and cancer predominantly comes from studies of workers, and relates to leukemia, particularly with 2 types called acute myeloid leukemia (AML) and to a lesser degree, chronic lymphocytic leukemia (CLL).” Exhibit I, American Cancer Society Webpage, available at http://www.cancer.org/docroot/PED/content/PED_1_3X_Benzene.asp?sitearea=PED.

An expert committee of the Institute of Medicine reviewed the epidemiological literature in 2003 and concluded that there was inadequate or insufficient evidence to determine whether an association between benzene exposure and multiple myeloma exists. Exhibit B, Mundt Report at 6.

Finally, The National Toxicology Program, under the auspices of the National Institute of Environmental Health and the National Institutes of Health, further confirms a link between benzene and AML and specifically states that no persuasive evidence links benzene and multiple myeloma:

Since benzene was reviewed for listing in the First Annual Report on Carcinogens and by the International Agency for Research on Cancer, numerous epidemiological studies of benzene exposure have been published. Some studies found that the risk of leukemia increased with increasing benzene exposure; increased risk of death from leukemia was very high in the groups with the highest exposure (IPCS 1993). . . . Most studies found that benzene exposure increased the risks of total lymphatic and hematopoietic cancer . . . including chronic lymphocytic leukemia, as well as acute myelogenous leukemia. *Little evidence was found for an association between benzene exposure and multiple myeloma or non-Hodgkin's lymphoma.*

Exhibit I, National Toxicology Program Benzene Assessment, available at <http://ntp.niehs.nih.gov/ntp/roc/eleveth/profiles/s019benz.pdf> (emphasis added) (internal citations omitted)

In short, despite the fact that benzene has been widely studied in numerous occupational contexts, no authoritative scientific or regulatory authoritative body, whether at the national or international level, has asserted that there is a causal link between benzene and multiple myeloma.

b. The Health Watch Cohort Study Found No Causal Association

For the past 27 years, the Australian Institute of Petroleum has sponsored studies to monitor the health of petroleum industry employees. Exhibit H, 2007 Health Watch 13th Report, at 3. 19,000 petroleum workers have been followed over time. *Id.* According to the latest statistical results, the investigators concluded that “the incidence [of multiple myeloma] is the same as that in the general population” and that “there is no significant excess of multiple myeloma in any work place type.” *Id.* at 68. Importantly, *no* myeloma cases were found among offshore production workers.² Exhibit H.

² Plaintiff's expert Dr. Infante only describes three studies, all of them inapplicable, that he alleges supports an association between crude oil benzene exposure and multiple myeloma. However, he neglects to discuss the Health Watch studies, which involve more comprehensive exposure data, and specifically include offshore workers like Plaintiff.

c. Multiple Other Studies Show No General Causation

Dr. Mundt elaborates on numerous studies involving thousands of occupationally exposed workers, stating that “studies of various chemical industry workers with benzene exposure, no significant increased risk of multiple myeloma has been reported.” Exhibit B, Mundt Report at 60. Further, “[l]ow-level exposures have not been convincingly linked with any human cancers including multiple myeloma. Exhibit B, Mundt Report at 5. Dr. Mundt also describes two meta-analyses, or a analyses involving a combination of studies. Exhibit B, Mundt Report at 6. In one of these meta-analyses, the results of 22 different studies of petroleum workers from the United States, Canada, the United Kingdom and Australia were combined, showing no statistically significant increase in the cases of multiple myeloma. Exhibit B, Mundt Report at 6 (describing Wong’s meta-analysis). Two of the largest cohorts of benzene exposure ever studied, the Pliofilm workers and the Chinese workers, show no increased risk of multiple myeloma. Exhibit C, Report of Ethan Natelson, M.D. (“Natelson Report”) at 3.

d. Scientific Reviews of the Literature Show No General Causation

The authoritative bodies discussed above review the relevant scientific literature when drawing conclusions about potential health effects. With respect to benzene, numerous reviews published by multiple scientists further confirm that the evidence does not support a general causation link between benzene and multiple myeloma. *See e.g.*, Bergsagelet, et al, *Benzene and Multiple Myeloma: Appraisal of the Scientific Evidence*, Journal of the American Society of Hematology vol. 94:4, August 1999 (attached as part of Exhibit H); Shewet Bwezabab, et al, *Does Benzene Cause Multiple Myeloma?: An Analysis of the Published Case-Control Literature*, Environmental Health Perspectives, vol. 104 supp. 6, December 1996 (attached as part of Exhibit H). Other reviews of the scientific literature are cited in the expert reports of two experts

retained by Shell Defendants, Dr. Kenneth Mundt (an epidemiologist) and Dr. Ethan Natelson (a hematologist). *See* Exhibits B and C.

e. The Epidemiology Is Supported By Clinical Evidence

Dr. Natelson, an expert hematologist who has treated thousands of patients with blood-related cancers, explains how the epidemiology coheres with medical reality, providing still further evidence against general causation. For example, cigarette smokers are exposed to benzene on a daily basis, but among cigarette smokers there is an increase of AML, but not multiple myeloma. Exhibit C, Natelson Report at 4. Dr. Natelson further states that the lack any evidence of an increased incidence of multiple myeloma is not surprising:

Aside from its industrial use, benzene is also an obsolete form of chemotherapy....[U]nder certain circumstances related to cumulative dose and duration of exposure, it is capable of producing a similar hematological toxicity to many modern chemotherapy drugs and radiation therapy in that it may cause a secondary form of [AML]. Thousands of such cases ... are reported in the medical literature. Yet, there is no observed companion syndrome of secondary [multiple myeloma] from any of these types of chemotherapeutic agents.

Exhibit C, Natelson Report at 4. Therefore, clinical medical realities reinforce the epidemiological findings: no reliable evidence support general causation of multiple myeloma and benzene exposure.

It is also a clinical truism that most cancers of the blood are idiopathic, or of no known cause. Exhibit C, Natelson Report at 3. When this is the case, a failure to rule out alternative idiopathic causes is also fatal to a causation opinion. *Henricksen*, No. CV-07-224-JLQ, at *25 (attached as part of Exhibit L). None of the Plaintiffs' experts have addressed the idiopathic nature of multiple myeloma,, or blood cancers generally, in their reports.

3. Specific Opinions of Plaintiff's Experts

a. Dr. Infante's Opinions

i. Dr. Infante's Interpretation of Epidemiology

Dr. Infante is a well-known epidemiologist with significant experience studying benzene and testifying in benzene toxic tort cases. Dr. Infante candidly admits that “[a]ssociations between benzene exposure and multiple myeloma have been difficult to determine.” Exhibit F, Infante Report, at 4. Dr. Infante also describes and acknowledges many of the studies that have found no statistically significant association between benzene and multiple myeloma. Exhibit F, Infante Report. However, Dr. Infante, contrary to the weight of the available evidence nevertheless opines that there is general causation between benzene and multiple myeloma.

Dr. Infante's opinion is founded upon inapplicable studies, including his own meta-analysis, that are inapposite to the facts of this case.³ In one key study that is relied upon by Dr. Infante involving upstream oil workers, there is no evidence of exposure to benzene. Instead, the Norwegian crude oil workers study, followed a cohort of approximately 27,000 workers classified using the Norwegian Registry of Employer and Employees as “offshore workers” and compared cases of cancer amongst this group with a group of approximately 370,000 workers from the general worker population. Kirkeleit et al, *Increased Risk of Acute Myelogenous Leukemia and Multiple Myeloma in a Historical Cohort of Upstream Petroleum Workers Exposed to Crude Oil*, Cancer Causes Control (Aug. 2007), 5 (hereinafter “the Norwegian crude oil workers study”) (Exhibit H). The researchers found an increased risk of AML and multiple

³ As *Daubert* and its progeny explain, proffered expert evidence must be both reliable and relevant. “Reliability is determined by assessing ‘whether the reasoning or methodology underlying the testimony is scientifically valid.’” But “relevance depends upon ‘whether [that] reasoning or methodology can be applied to the facts at issue.’” *Knight v. Kirby Inland Mar., Inc.*, 482 F.3d 347, 358 (5th Cir. 2007) (citing *Daubert v. Merrell Dow Pharm.*, 509 U.S. 579, 592-93 (1993)).

myeloma among the offshore workers. This study does not actually measure any benzene exposure. The association is between employment status and cancer, not any chemical and cancer. The authors readily admit this weakness inherent in the study design, stating that a lack of exposure figures for benzene is a major limitation. Exhibit H, Norwegian crude oil workers study at 5. Instead, the authors only “suggest that benzene exposure . . . resulted in an increased risk of multiple myeloma.” Exhibit H, *Kirkeleit* at 5. A “suggestion” of a causal connection is insufficient for admissibility in federal court. *See Knight*, 482 F.3d at 353 (explaining that a study finding an increased cancer risk among truck drivers may “suggest” a relation between cancer and diesel exposure but did not “clearly support” that conclusion).

Similar critiques apply to the few additional studies Dr. Infante identifies as support for his opinion that crude oil or natural gas exposure causes multiple myeloma. The Delzell study of Union Oil workers mentioned by Dr. Infante is an unpublished study. Nevertheless, this study is a case/control study that does not appear to describe actual benzene exposure. The Divine and Hartman Texaco crude oil workers study suffers from a similar limitation. Divine and Hartman, however, also note that petroleum workers are healthier than the general population. The mortality due to multiple myeloma was only slightly higher than expected, with a far larger increase in mortality being attributed to AML. *See* Exhibit H, Divine and Hartman study. The authors of the United Kingdom gas workers study note that the deaths from multiple myeloma they observed could have been a chance finding. Exhibit F, Infante Report at 14. Finally, the Hansen study cited by Infante involves Danish stokers of coal and oil fueled furnaces and is inapplicable to Plaintiff. *Id.*

Dr. Infante also relies heavily on his own meta-analysis in which he found an association between benzene exposure and multiple myeloma based on a small grouping of selected studies.

Given that his meta-analysis only includes seven studies, as opposed to Wong's 22 studies (see Exhibit B, Mundt Report at 6), and neglects to include studies with the largest negative associations, it is of little value in a courtroom setting.

Dr. Infante's meta-analysis results have not been replicated by other scientists. "Rarely, if ever, does a single study conclusively demonstrate a cause-effect relationship. It is important that a study be replicated in different populations and by different investigators before a causal relationship is accepted by epidemiologists and other scientists." Exhibit G, Reference Manual, 377; *see Havner*, 953 S.W.2d at 727 (stating that more than one study is needed).

Dr. Infante's study has actually been contradicted by two other meta-analyses. As stated by Dr. Mundt:

Two meta-analyses found no evidence for an association between petroleum and solvent exposures and risk of multiple myeloma: an analysis of 22 cohort studies on petroleum workers (Wong 1997) and an analysis of 7 case-control studies on occupational exposure to benzene or solvents (Sonoda 2001). A third analysis pooled results from seven cohort studies not including petroleum workers, one of which - the Pliofilm study - was the only study with a statistically significant results, based on 4 cases. (Infante 2006).

See Exhibit B, Mundt Report at 6. Dr. Infante's findings are also contradicted by the findings of multiple international and national scientific authoritative bodies. Finally, Infante's meta-analysis, which does not include studies involving workers exposed to crude oil or other fuel sources, but includes workers exposed to almost pure benzene, is inapplicable to Plaintiff's case here.

ii. Dr. Infante's biological plausibility theory should be excluded

Dr. Infante also opines that a causal link between benzene and multiple myeloma is biologically plausible. As an epidemiologist rather than toxicologist or clinical researcher, Dr. Infante is not qualified to opine on the significance of hemotoxicity and genetic damage as

support for a conclusion that benzene causes multiple myeloma, a particular type of cancer.⁴ Irrespective of Dr. Infante's qualifications, however, his biological plausibility theory is of minimal relevance given the breadth and scope of the human studies that find no significant association. The Fifth Circuit has held that evidence of genetic damage alone, without other scientific evidence, is insufficient. *Allen*, 102 F.3d at 198. In rejecting a theory that ethylene oxide could cause brain cancer just because it had mutagenic and genotoxic effects, the Fifth Circuit stated that "an effect on living cells or genes is the beginning, not the end of the scientific inquiry and proves nothing about causation without other scientific evidence." *Allen*, 102 F.3d at 198. In this case, vastly more conclusive epidemiology contradicts Dr. Infante's biological plausibility theory. *See Allen*, 102 F.3d at 197 (the most useful and conclusive type of general causation evidence is epidemiology). Dr. Infante's biological plausibility theory is unreliable and should be excluded.

b. Dr. Harrison's Opinions

Dr. Harrison, an occupational medicine doctor, primarily offers opinions with respect to specific causation, including his review of Plaintiff's medical history. His general causation opinions are based on the same literature, including the inapplicable the Norwegian crude oil workers study, relied upon by Dr. Infante. *See Exhibit E, Report of Robert Harrison, M.D., M.P.H.* Because Dr. Harrison's opinions are based on selected inapplicable studies that contradict the vast majority of the epidemiology literature and the findings of international and national scientific authorities, his general causation opinion should be excluded pursuant to Rule 702.

c. Dr. Butler's Opinions

⁴ By contrast, Dr Pyatt, a toxicologist, opines that benzene exposure is not a biologically plausible cause of multiple myeloma. *See Exhibit J, Pyatt Report at 9-10.*

Dr. Butler, as a pathologist rather than a toxicologist or epidemiologist is not qualified to offer a general causation opinion. Fed. R. Civ. Evid. 702, *see also* Exhibit D, Report of Sheila Butler, M.D. Nevertheless, her general causation opinion, like those of Dr. Infante and Dr. Harrison, is based on her reliance on inapplicable studies that contradict the epidemiology literature and findings of international and national scientific authorities. For the same reasons, her general causation opinion should be excluded. Finally, since Dr. Butler did not adequately account for an idiopathic cause of Plaintiff's multiple myeloma, her specific causation opinion is also unreliable.

VII. CONCLUSION

The expert opinions of Dr. Infante, Dr. Harrison, and Dr. Butler should be excluded. Their causation opinions are neither relevant nor reliable. Further, without evidence of general causation, any specific causation opinions are simply irrelevant. Pursuant to Federal Rule of Evidence 702, Shell Defendants request that Dr. Infante, Dr. Harrison and Dr. Butler be excluded from testifying in this case and that their expert opinions be found inadmissible.

For the reasons stated in this motion, Shell Defendants respectfully request that this Court enter an order granting Shell Defendants Motion to Exclude Plaintiff's Causation Experts, and any other relief this Court deems just and proper.

Respectfully submitted,

/s/

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CERTIFICATE OF SERVICE

I hereby certify that on this 17th day of February 2009, a true and correct copy of the *Shell Defendants' Brief in Support of Their Motion to Exclude Plaintiff's Causation Experts* was electronically filed with the Clerk of the Court and served on all parties of record using the CM/ECF System.

/s/ Stan Perry
STAN PERRY

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